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THE SCRIPPS RESEARCH INSTITUTE
10550 NORTH TORREY PINES ROAD
MAIL DROP TPC 8
LA JOLLA, CA 92037

EXAMINER	
DAVIS, MINH TAM B	

ART UNIT	PAPER NUMBER
1642	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/277,064	SHERMAN, LINDA A.	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 61-75* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 61-75* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The finality of the previous Office action has been withdrawn, and the prosecution of this application is reopened based on new consideration, and in view that the enablement issue has been overcome.

It is noted that applicant has paid for a Notice of Appeal. Applicant can either request a refund or place the funds on credit for future appeals.

Accordingly, claims 1, 61-75 are being examined.

NEW REJECTIONS BASED ON NEW CONSIDERATION

Claim Rejections - 35 USC § 112, Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 61-68, 73, 75 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 61-68, 73, 75 are drawn to:

1) A method for treating a tumor expressing a Her-2/Neu protein, comprising administering a polypeptide "having" the amino acid sequence SEQ ID NO:12 (claims 61-62).

2) The method of claim 61, wherein said polypeptide is linked to a carrier (claim 63), or is administered as a homopolymer (claim 64).

3) The method of claim 1 or 61, further comprising administering a second component, which primes cytotoxic T lymphocytes for activation, wherein the second component could "comprise" tripalmitoyl-S-glycerylcysteinyl-seryl-serine (P3CSS) (claims 65-66, 73).

4) The method of claim 1 or 61, further comprising administering a second polypeptide, which could "comprise" SEQ ID NO:9 (claims 67-68, 75).

The specification discloses that SEQ ID NO:12 (peptide H7 on table 6 on page 103), consisting of 10 amino acids in length, could produce CTLs specific for Her-2/neu when injected into A2.1 transgenic mice, wherein said CTLs could lyse several human cancer cell lines derived from various cancers in vitro (Example 5, on pages 103-108, and table 7 on page 107). Further, in the response of 02/14/06, Applicant submits a reference by Lustgarten et al, 2004, Eur J Immunol, 34: 752-761, showing that SEQ ID NO:12 (p.760, para under item 4.4) induces CTLs in transgenic mice expressing the antigen Her-2/neu (p.753, second column, paragraph under item 2.2), wherein said CTLs, when isolated and transferred to mice with mammary cancer (p.759, second column, paragraph under item 4.1), could reduce growth of said cancer (p.754, second column, paragraph under items 2.4, bridging p.755). Further, the specification discloses

that the peptide consisting of SEQ ID NO:9 induces CD4 T cell helper response (p.79, lines 9-12).

It is noted that because SEQ ID NO:12 consists of only 10 amino acids in length, and because of the language "a polypeptide having" of claim 61, which is reasonably interpreted as the same the open language "comprising", Claims 61-68 encompass a method for treating any cancer expressing Her-2/Neu protein, by administering **a polypeptide comprising "unknown sequences attached to the 10 amino acid peptide SEQ ID NO:12".**

Although the peptide consisting of SEQ ID NO:12 is correlated with activating CTLs and treating breast cancer overexpressing Her-2/neu, there is no correlation between structure of the claimed genus of polypeptides "having" SEQ ID NO:12, i.e. having unknown sequences attached to SEQ ID NO:12, and the function of activating CTLs specific for Her-2/neu or the function of treating tumor expressing Her-2/neu, because one cannot predict that the peptide SEQ ID NO:12 is even exposed on the surface of the claimed polypeptide "having" SEQ ID NO:12, such that it is recognized by CTLs specific for SEQ ID NO:12, and because one cannot predict that CTLs specific for the claimed genus of polypeptides would recognize Her-2/neu, due to the unknown effect of the attached sequence on the conformation of the claimed polypeptides. It is well known in the art that a protein conformation or its three-dimensional structure depends on its amino acid composition. Bowie et al (Science, 1990, 257:1306-1310, of record) teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function and carry out the instructions of the genome and further teaches that the problem of predicting protein structure from sequence data and in turn utilizing predicted

structural determinations to ascertain functional aspects of the protein is extremely complex. (col 1, p. 1306). Bowie et al further teach that while it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (col 2, p. 1306).

Further, due to the open language "comprises" in claims 66, 73, claims 66, 73 encompass method for activating cytotoxic T lymphocytes in any cancer patient, or for treating any cancer, wherein the cancer expresses Her-2/Neu protein, by administering a polypeptide comprising SEQ ID NO:12, and further **administering a second component comprising "unknown sequences attached to P3SCC".**

In addition, because SEQ ID NO:9 consists of only 13 amino acids in length, and because of the open language "comprises" in claims 68, 75, claims 68, 75 encompass method for activating cytotoxic T lymphocytes in any cancer patient, or for treating any cancer, wherein the cancer expresses Her-2/Neu protein, by administering a polypeptide comprising SEQ ID NO:12, and further **administering a second polypeptide comprising "unknown sequences attached to the peptide SEQ ID NO:9".**

Although drawn to DNA arts, the findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli

Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula, [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials." Id. At 1567, 43 USPQ2d at 1405. The court also stated that

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. Id. At 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id.

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that □the written description requirement can be met by "show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with

a known or disclosed correlation between function and structure, or some combination of such characteristics." Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The inventions at issue in Lilly and Enzo were DNA constructs per se, the holdings of those cases are also applicable to claims such as those at issue here. A disclosure that does not adequately describe a product itself logically cannot adequately describe a method of using that product.

In this case, the specification does not describe a polypeptide comprising SEQ ID NO:12 or 9, or a component comprising P3SCC in a manner that satisfies either the standards as shown in the example of Lilly or Enzo. The specification does not provide sufficient structure or common structure of the claimed genus of polypeptides comprising SEQ ID NO:12 or 9, or the claimed genus of components comprising P3SCC to support the broad breath of the genus claimed, other than SEQ ID NO:12, or 9 or P3CSS. Nor is there any functional characteristics coupled with a known or disclosed correlation between structure and function. Although the specification discloses a single peptide consisting of SEQ ID NO:12, or 9 or P3CSS, this does not provide a description of a genus of polypeptides "comprising" SEQ ID NO:12 or 9, or a genus of component comprising P3SCC, that would satisfy the standard as shown in the example of Enzo.

The specification also fails to describe a polypeptide comprising SEQ ID NO:12 or 9, or a component comprising P3CSS, by the standards shown in the example in Lilly. The specification describes only a single peptide consisting of SEQ ID NO:12, or 9 or P3CSS. Therefore, it necessarily fails to describe a "representative number" of such species. In addition,

the specification also does not describe "structural features common to the members of the genus, which features constitute a substantial portion of the genus."

The specification does not provide an adequate written description of a polypeptide comprising SEQ ID NO:12 or 9, or a component comprising P3CSS, that is required to practice the claimed invention, and one of skill in the art would reasonably conclude that Applicant did not have possession of the claimed genus of polypeptides comprising SEQ ID NO:12 or 9, or the claimed genus of components comprising P3SCC at the time the invention was made.

Thus, the specification does not meet the 112, first paragraph written description requirement. Since the specification fails to adequately describe the product for use in the claimed method, it also fails to adequately describe the claimed method.

Claim Rejections - 35 USC § 112, Scope of Enablement

Claims 1, 61-75 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for activating specific cytotoxic T lymphocytes in vivo in an animal having a "breast cancer that overexpresses" a Her-2/Neu protein, or a method for treating "a breast cancer that overexpresses" a Her-2/Neu protein, comprising administering a polypeptide "consisting of" SEQ ID NO:12, wherein a second component "consisting of" P3CSS or a second polypeptide "consisting of" SEQ ID NO:9 could be also administered, does not reasonably provide enablement for a method for activating specific cytotoxic T lymphocytes in vivo in an animal having malignant cells that **"expresses"** a Her-2/Neu protein, or a method for treating **"any tumor"** that **"expresses"** a Her-2/Neu protein, comprising administering a polypeptide **"having"** SEQ ID NO:12, wherein a second component

"comprising" P3CSS or a second polypeptide **"comprising"** SEQ ID NO:9 could be also administered. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1, 61-75 are drawn to:

1) A method for activating cytotoxic T lymphocytes in vivo in an animal having malignant cells that express a Her-2/Neu protein, or a method for treating a tumor expressing a Her-2/Neu protein, comprising administering the polypeptide of SEQ ID NO:12 or a polypeptide having the amino acid sequence SEQ ID NO:12 (claims 1, 61-62, 69).

2) The method of claim 1 or 61, wherein said polypeptide is linked to a carrier (claims 63, 70), or is administered as a homopolymer (claims 64, 71).

3) The method of claim 1 or 61, further comprising administering a second component, which primes cytotoxic T lymphocytes for activation, wherein the second component could comprise tripalmitoyl-S-glycerylcysteinyl-seryl-serine (P3CSS) (claims 65-66, 72-73).

4) The method of claim 1 or 61, further comprising administering a second polypeptide, which could comprise SEQ ID NO:9 (claims 67-68, 74-75).

The following *Wands* factors have been considered when the 112, first paragraph, scope of enablement rejection was made.

The breadth of the claims

The breadth of the claims is broad.

Because SEQ ID NO:12, and SEQ ID NO:9 consist of only 10 and 13 amino acids in length, respectively, and further because of the language "a polypeptide having" of claim 61, and "comprises" of claims 66, 68, 73, 75, the claims encompass a method for activating CTLs in vivo or a method for treating cancer, using **unknown sequences attached to the 10 amino acid peptide SEQ ID NO:12** (claims 61-68), and further **using unknown sequences attached to P3Scc** (claims 66, 73), or **unknown sequences attached to the 13 amino acid peptide SEQ ID NO:9** (claims 68, 75), wherein the effect of the unknown sequences on the function of the claimed sequences cannot be predicted.

Further, due to the language "express", and due to the fact that Her-2/neu is a self-antigen, which is expressed in normal tissues, the claims 1, 61-75 encompass a method for activating CTLs in vivo in **any cancer**, or a method for treating **any cancer** in a patient, wherein said cancer **expresses Her-2/Neu at any level**, which is not necessarily higher than that of normal cells, and which is not necessarily in sufficient quantity to be recognized and lysed by CTLs.

In addition, the claims 61-68 encompass a method for **treating any type of abnormal growth**, which is not necessarily cancer, in view that "a tumor" encompasses any enlargement or abnormal growth, which is not necessarily cancerous, for example, cystic of the pancreas, splenic tumor or enlargement of the spleen, etc... (Stedman's medical dictionary, 25th ed, 1990, p.1652-1653, of record).

The nature of the invention

The nature of the invention is complex. Although administration of the peptide consisting of SEQ ID NO:12 activates CTLs in vivo is disclosed in the specification, however, the claims encompass a method for activating CTLs in vivo in any cancer patient, or a method for treating any cancer or any abnormal growth, that expresses Her-2/neu at any level, using unknown sequences attached to the 10 amino acid peptide SEQ ID NO:12, or unknown sequences attached to P3Scc or the peptide SEQ ID NO:9, wherein the effect of the unknown sequences on the function of the claimed sequences cannot be predicted, and wherein a successful treatment of any cancer or any abnormal growth, that expresses Her-2/neu at any level cannot be predicted.

The state of the prior art

Although the prior art (WO 94/20127, see 102 rejection below) teaches administration of SEQ ID NO:12 into cancer patients, the prior art is silent concerning using a polypeptide that is longer than SEQ ID NO:12, or P3SCC or SEQ ID NO:9, which encompasses unknown sequences attached to the 10 amino acid peptide SEQ ID NO:12, or unknown sequences attached to P3Scc or the peptide SEQ ID NO:9. Further, although the prior art (WO 94/20127, see 102 rejection below) teaches administration of SEQ ID NO:12 into cancers, such as prostate cancer, cervix carcinoma, and kidney carcinoma, which inherently overexpress Her-2/neu, the art is silent concerning treating any cancer that expresses Her-2/neu at any level, or treating any abnormal growth.

The level of one of skill in the art

Although the level of skill in the field of molecular pathology is high, it would be undue experimentation for one of skill in the art to practice the claimed invention.

The level of predictability of the art

The level of unpredictabililty is high.

One cannot predict that the peptide SEQ ID NO:12 is even exposed on the surface of the claimed polypeptide "having" SEQ ID NO:12, such that it is recognized by CTLs specific for SEQ ID NO:12, because SEQ ID NO:12 is only 10 amino acid in length, and because of the unknown effect of the attached sequences to the conformation and function of the claimed polypeptide, in view of the teaching in the art that a protein conformation or its three-dimensional structure and its function depend on its amino acid composition, as taught by Bowie et al (Science, 1990, 257:1306-1310, of record), supra.

Similarly, in view of the teaching of Bowie et al, one cannot predict whether the claimed polypeptide comprising SEQ ID NO:9 or P3CSS would function as claimed.

Further, one cannot predict that any cancer that expresses Her-2/Neu at any level could be successfully treated by the claimed method, in view that Her-2/Neu is a self-antigen, and if the cancer expressed Her-2/Neu at the same level as that of normal tissues, the CTLs cannot distinguish between target cancer cells and normal cells, and thus the claimed method would not be specific for cancer cells. Further, one cannot predict that any malignant cells that "express" a Her-2/Neu protein, or any tumor cells that "express" a Her-2/Neu protein at any level would have adequate amount of Her-2/Neu protein, such that they could be recognized and lyzed by

CTLs that are specific for the Her-2/neu peptide SEQ ID NO:12. This possible problem with insufficient quantity of SEQ ID NO:1 expressed on malignant cells could further be exacerbated, in view that cancer cells could downregulate the expression of tumor antigens, and thus reducing the amount of the antigens presented, and consequently the possibility of being recognized and lysed by CTLs, and further in view of the well-known cancer tolerance phenomena. For example, White et al, 2001, Ann Rev Med, 52: 125-145, teach that antigen internalization or downregulation can cause repeat dosing to be unsuccessful due to the disappearance of the antibody target (p.126, paragraph before last).

Moreover, although CTLs induced by SEQ ID NO:12 and specific for Her-2/neu could be used for treating one single cancer overexpressing Her-2/neu in mice, i.e. breast cancer, as taught by Lustgarten et al, supra, could one cannot predict a successful therapy, wherein the cells to be treated are any cancer cells or any tumor cells that express Her-2/neu, which are not necessarily cancerous, and are unrelated to cancer, and having different etiology and characteristics than breast cancer cells, and would not predictably response to the administration of SEQ ID NO:12, or have the same response as breast cancer.

Existence of working example, and the amount of direction provided by the inventor

The specification only discloses one example of a method for activating CTLs using the peptide "consisting of" SEQ ID NO:12.

The specification does not disclose a method for activating CTLs using a peptide longer than SEQ ID NO:12, or SEQ ID NO:9 or P3CSS, which encompasses unknown sequences attached to the 10 amino acid peptide SEQ ID NO:12, or unknown sequences attached to P3Scc

or the peptide SEQ ID NO:9, wherein the effect of the unknown sequences on the function of the claimed sequences cannot be predicted. The specification does not disclose that CTLs specific for the sequence comprising unknown sequences attached to the 10 amino acid peptide SEQ ID NO:12, would recognize and lyse any tumor cells that express Her-2/neu. The specification does not disclose how to treat any cancers that express Her-2/Neu at any level, or how to treat any abnormal growth, that express Her-2/Neu at any level, which is not necessarily cancer.

It is noted that MPEP 2164.03 teaches that "the amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability of the art. In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The amount of guidance or direction refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature ot the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to explicitly stated in the specification. In constrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as how to make and use the invention in order to be enabling."

Given the above unpredictability, and in view of the complex nature of the invention, and a lack of sufficient disclosure in the specification, it would be undue experimentation for one of skill in the art to practice the claimed invention.

Claim Rejections - 35 USC § 102(b)

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 61-67, 69-74 are rejected under 35 U.S.C. 102(b) as being anticipated by Grey H M et al (WO 94/20127, 09/15/1994, of record).

Claims 1, 61-67, 69-74 are drawn to:

1) A method for activating cytotoxic T lymphocytes in vivo in an animal having malignant cells that express a Her-2/Neu protein, or a method for treating a tumor expressing a Her-2/Neu protein, comprising administering the polypeptide of SEQ ID NO:12 or a polypeptide having the amino acid sequence SEQ ID NO:12, wherein the polypeptide could be incorporated into a pharmaceutical composition further comprising a pharmaceutiacally acceptable carrier (claims 1, 61-62, 69).

2) The method of claim 1 or 61, wherein said polypeptide is linked to a carrier (claims 63, 70), or is administered as a homopolymer (claims 64, 71).

3) The method of claim 1 or 61, further comprising administering a second polypeptide or a second component, which primes cytotoxic T lymphocytes for activation, wherein the second component could comprise tripalmitoyl-S-glycerylcysteinyl-seryl-serine (P3CSS) (claims 65-67, 72-74).

WO 94/20127 teaches epitopes from a desirable antigen, particularly those associated with human cancers for which the amino acid sequence of the potential antigen target is known

(p.6, lines 2-10). WO 94/20127 teaches that pharmaceutical composition comprising the peptide of the invention is administered to a patient already suffering from cancer to elicit an effective CTL response to the tumor antigen, to cure or at least partially arrest symptoms and/or complications (p.22, lines 5-15). WO 94/20127 teaches that examples of diseases include prostate cancer, renal carcinoma, cervical carcinoma, lymphoma (p.21, last paragraph, bridging p.22). WO 94/20127 teaches that it may be desirable to include in the pharmaceutical compositions of the invention at least one component which primes CTL, such as P3CSS (p.19, last paragraph, bridging p.20). WO 94/20127 teaches that the lipidated peptide that primes CTLs can be injected directly in a micellar form, or emulsified in an adjuvant (p.19, lines 31-33). WO 94/20127 further teaches that the peptide may be introduced into a host, including humans linked to its own carrier or as a homopolymer or heteropolymer of active peptide units (p.26, lines 8-22). WO 94/20127 teaches that the vaccines can also contain a physiologically tolerable (acceptable) diluent such as water, phosphate buffered saline (p.26, lines 23-25).

One of the peptide taught by WO 94/20127, peptide 1.0738, from the antigen c-ERB2, in Appendix II, page 108, is the same as the claimed SEQ ID NO:12.

In addition, it is noted that the lipidated peptide taught by WO 94/20127 is the same as the second polypeptide of claims 67, 74.

Further, although WO 94/20127 does not teach that human prostate cancer, cervix carcinoma, and kidney carcinoma overexpress Her-2/neu, it is well known in the art that human prostate cancer, cervix carcinoma, and kidney carcinoma, all overexpress c-erb-2, which is the same as Her-neu-2/neu (Gu K et al, Cancer letters, Feb 6, 1996,99(2): p185-9; Costa MJ et al,

American J Clin Pathol,1995, v.104, n.6, p:634-642; and Danova M et al, European journal of histochemistry, 1992, 36(3): p279-88).

Although the art is silent concerning the actual data on the effect of administrating the peptide pharmaceutical composition into patients having prostate cancer, cervix carcinoma, or kidney carcinoma, however, because the method of the prior art comprises the same method steps as claimed in the instant invention using the same composition, the claimed method is anticipated because the method will inherently lead to the claimed effects. See Ex parte Novitski 26 USPQ 1389 (BPAI 1993).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 68, 75 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 94/20127, in view of US 6,419,931.

Claims 68, 75 are drawn to:

A method for specifically activating CTLs in vivo, or treating a tumor expressing a Her-2/Neu protein, comprising administering a polypeptide having the amino acid sequence SEQ ID NO:12, further comprising administering a second polypeptide, wherein the second polypeptide comprises SEQ ID NO:9.

The teaching of WO 94/20127 has been set forth above. In addition, WO 94/20127 further teaches that the ability of the peptide of the invention to induce CTL can be enhanced by linkage to a sequence which contains at least one epitope that is capable of inducing a T helper cell response, which in some embodiments, is one that is recognized by T helper cells in the majority of the population (p.18, lines 15-33). WO 94/20127 teaches that example of T helper peptides include tetanus toxoid 830-843, influenza 307-319, malaria 382-398, and 378-389.

WO 94/20127 does not teach that the T helper peptide is SEQ ID NO:9.

US 6,419,931 teaches a T helper epitope for use with a CTL epitope peptide, such as a CTL epitope of a tumor antigen to induce a CTL response to said antigen (column 4,under Summary of the invention). One of the T helper epitopes taught by US 6,419,931(peptide 875.23 in the first table in columns 29-30) is the same as the claimed SEQ ID NO:9. US 6,419,931 teaches that the T helper inducing peptide could be linked or not linked with the CTL epitope peptide (column 4, lines 15-28).

It would have been obvious to replace the T helper inducing peptide taught by WO 94/20127 with the T helper inducing peptide taught by US 6,419,931, and to include the T helper peptide in a second step of administration, because one would have expected that a T helper inducing peptide administered together or separately from the peptide taught by WO 94/20127 would induce T helper response, and enhance the CTL response, in view of the teaching of WO 94/20127.

One would have been motivated to include a second peptide, SEQ ID NO:9, in the method taught by WO 94/20127, with a reasonable expectation of success of enhancing the CTL response to the peptide taught by WO 94/20127.

Further, although the art is silent concerning the actual data on the effect of administrating the peptide pharmaceutical composition into patients having prostate cancer, cervix carcinoma, or kidney carcinoma, however, because the method of the combined prior art comprises the same method steps as claimed in the instant invention using the same composition, one would have expected that the method taught by the combined prior art will lead to the claimed effects. See Ex parte Novitski 26 USPQ 1389 (BPAI 1993).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 571-272-0830. The examiner can normally be reached on 9:00 AM-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, JEFFREY SIEW can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER

MINH TAM DAVIS
April 17, 2006